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Alteration of Laser-Tissue Interaction With the 805 nm Diode Laser Using Indocyanine Green in the Canine Prostate

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Background and Objective: **Research interests in laser prostatectomy continue to evaluate a variety of wavelengths and treatment parameters in an effort to optimize treatment. Recently, a semiconductor diode laser with a wavelength of 805 nm has become available for clinical use; however, free-beam noncontact applications were limited by the low power output (25 W). In this study in the canine prostate, the possible potentiating effects of intravenously administered indocyanine green (ICG) were evaluated with the 805 nm diode laser.**

Study Design/Materials and Methods: **A total of 16 fixed position, free-beam lasings were performed at 25 W for 60 sec in four dogs with eight lasings before and eight lasings after ICG administration. Endoscopic observations and measurements of lesion volumes were used to evaluate the laser-tissue interactions.**

Results: **Prior to ICG administration, we observed that side fire irradiation produced primarily small coagulative lesions. Following ICG administration, however, immediate and more noticeable tissue vaporization occurred, although total lesion size was not increased. Pathologic review demonstrated less coagulation and hyperemia, but a larger vaporized cavity in the ICG treated tissue.**

Conclusion: **These findings suggest intravenous ICG alters laser-tissue interaction with the 805 nm diode laser in the canine prostate. The use of the 805 nm diode laser with enhancing chromophores deserves further investigation.**

Key words: chromophores, diode laser, indocyanine green, laser prostatectomy, laser-tissue interactions

INTRODUCTION

Laser prostatectomy is evolving as a viable alternative to transurethral electrosurgical prostatectomy. As experience with laser prostatectomy expands, the strengths and limitations of the currently available techniques, laser devices, and fibre delivery systems become more apparent. In addition, evaluation of laser wavelengths other than Nd:YAG (1064 nm) are ongoing. Recently, a gallium arsenide semiconductor diode laser with a wavelength of 805 nm was applied to a variety of urologic conditions using a contact delivery system [1]. Noncontact, free-beam, side fire irradiation, however, has been limited by its low power output of 25 W [2].

The use of chromophores have been shown to enhance or alter laser-tissue interactions with other wavelengths [3]. Previous investigators have demonstrated that laser-tissue interactions

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using the 805 nm diode laser on rat liver were significantly potentiated with the addition of the chromophore indocyanine green (ICG) [4]. In this study we evaluated the laser-tissue effects in the canine prostate with the 805 nm diode laser using a free beam irradiation technique and intravenous administration of ICG.

Indocyanine green (ICG) is a watersoluble tricarbocyanine dye with a peak absorption ~800–810 nm when dissolved in blood, plasma, and bile [5]. When given intravenously, ICG becomes rapidly and almost entirely bound to plasma protein, of which albumin is the principle carrier [6]. Within 20 min of administration, only 4% of the agent remains in plasma [6]. Elimination occurs through hepatic clearance with the dye being excreted into bile in an unconjugated form. There is no significant renal excretion or tissue uptake of ICG [6].

Established clinical uses for indocyanine green in the past have included the measurement of hepatic blood flow, estimation of cardiac output and in ophthalmic angiography [7]. ICG has been found to be safe for use in humans with a reported incidence of clinically significant adverse events occurring in 1 in 30–40,000 administrations [8,9]. Most side effects have been related to iodine sensitivity in susceptible individuals. It has been theorized that slow infusion of ICG may be associated with fewer adverse reactions than a single bolus injection [10].

MATERIALS AND METHODS

Four adult male beagles, each weighing between 10–15 kg, underwent open suprapubic cystotomy and perineal urethrostomy under general anesthesia in accordance with a protocol approved by the Institutional Animal Care and Use Committee (IACUC). A 21 Fr rigid cystourethroscope with a 30° lens was attached to a video camera advanced retrograde through the perineal urethrostomy and into the prostatic fossa. The Diomed (Cambridge, UK) 805 nm wavelength diode laser was used in this study. Laser energy was delivered with a Dornier (Dornier Medical Systems, Kennesaw, GA) 600 μm SideFocus II lateral fire laser fiber in two animals, and the Bard (C.R. Bard, Covington, GA) Urolase fiber was used in two different animals. The laser fiber during each lasing was advanced antegrade through the bladder neck into the prostatic fossa aided by endoscopic guidance. The tip of the laser fiber was kept fixed ~2 mm away from the prostatic tissue during all lasings. In all animals, the left lateral lobe of the prostate was treated prior to the administration of indocyanine green inorder to serve as a control. The probe was first advanced to the left apex of the prostate. Fixed position lasing was then initiated at 25 W for 60 sec under videoendoscopic monitoring and continuous room temperature water irrigation. The fiber was then withdrawn to the left base of the gland and the lasing repeated. Indocyanine green (ICG) (Becton Dickinson Microbiology Systems, Cockeysville, MD) at a dose of 10 mg/kg was then administered intravenously over 1 min via an external jugular intravenous cutdown line.

Four min after infusion of ICG, lasing of the right apical region was performed at 25 W for 60 sec. At 5.5 min postinfusion of ICG, lasing was repeated at the right base. The animals were then euthanized and the prostate removed. The prostate glands were sectioned transversely at 2–3 mm intervals. Coagulation zones and vaporized cavities if present were measured in three dimensions and the values used for volume calculations.

RESULTS

Table 1 summarizes the laser-tissue interactions as evaluated by the observed endoscopic changes during lasing and the gross pathologic findings. The left side of each prostate underwent laser irradiations prior to ICG administraion. In general, these control irradiations produced coagulation necrosis; vaporization, often with tissue charring, was rare. A representative example of the endoscopic appearance following control lasings is displayed in Figure 1.

Following the intravenous administration of ICG, endoscopic observations during lasing revealed more immediate tissue changes in comparison to those sites treated before ICG. In addition, tissue vaporization and carbonization were more prominent features of the laser-tissue interaction. These observations were noted with both laser fibers and at both the 4 min and 5.5 min irradiation times. An example of the site of lasing post-ICG administration as it appeared endoscopically is shown in Figure 2.

The mean prostatic weight was 17 g (range 10–22.6 g). Gross inspection of the prostates was performed and calipers used to measure the size of the coagulative zones and vaporized cavities at the site of each lasing. The volume of each coagulative and vaporized lesion was calculated based on the formula for a prolate ellipse. ($V = L \times W \times H \times$

TABLE 1. Endoscopic Observations During Lasings

Dog	Laser fiber	Treatment site[a]	Findings
1	SideFocus	LA(−ICG)	coag
		LB(−ICG)	coag
		RA(+ICG)	char + vaporiz
		RB(+ICG)	char + vaporiz
2	SideFocus	LA(−ICG)	coag + vaporiz(40s)
		LB(−ICG)	coag + popcorn vaporiz(50s)
		RA(+ICG)	vaporiz(5s)
		RB(+ICG)	vaporiz(immediate)
3	Urolase	LA(−ICG)	coag
		LB(−ICG)	coag
		RA(+ICG)	popcorn(immediate)
		RB(+ICG)	popcorn(immediate)
4	Urolase	LA(−ICG)	popcorn (50s)
		LB(−ICG)	popcorn (40s)
		RA(+ICG)	popcorn (10s)
		RB(+ICG)	vaporiz throughout lasing

[a]LA = Left apex; LB = Left base; RA = Right apex; RB = Right base.

0.523) A compilation of the mean dimensions and volumes of the coagulative and vaporized lesions for each fiber is displayed in Table 2. The range, mean, and standard deviation values for the volumes of coagulation and vaporized lesions are shown in Tables 3 and 4, respectively. P value determinations were performed using the Student's t-test. A P value of <0.05 was considered significant. The mean volume of the coagulation zones was not significantly different when the sites of lasing prior to or after ICG administration were compared ($P = 0.81$). A comparison of the mean volume of the vaporized cavities, however, revealed a statistically significant increase in those sites lased after ICG administration ($P = 0.015$). However, the large standard deviation diminishes the strength of this observation. A representative section encompassing lesions created before and after ICG administration is shown in Figure 3. The larger area of vaporization and smaller coagulative zone is clearly evident on the ICG treated side.

DISCUSSION

Semiconductor diode lasers have had extensive use in the electronic and telecommunication industries [11]. Recently, diode lasers have been developed with clinical applications. These lasers are compact, do not require special electrical connections, and are less expensive than previously available surgical lasers.

A variety of procedures have been performed with these lasers in ophthalmology, gynecology, and plastic surgery [12–14]. In urology an 805 nm diode laser has been used in a variety of contact procedures, including circumcision, orchidectomy, and hydrocele repairs replacing the scalpel as the cutting tool [1]. This device was also used in endoscopic urologic procedures for the treatment of urethral strictures, bladder tumors, benign prostatic hyperplasia, and in laparoscopy [1].

Initial clinical experience with the 805 nm diode laser in contact applications suggested similar tissue interactions as the Nd:YAG [11]. A comparison between the Nd:YAG and the 805 nm diode laser in contact mode at low power and short irradiation times confirmed these initial observations [2]. In noncontact delivery however, a greater degree of absorption was noted when the diode laser was used in blood and pigmented tissue limiting the depth of tissue penetration [11].

The use of chromophore dyes has been explored as a method of modifying tissue effects produced by certain laser wavelengths [3]. Chromophores are optically active material (usually colored) that act as an absorbing medium for laser light within tissue. By using a chromophore that absorbs a specific laser wavelength, energy absorption is enhanced, whereas transmission and scatter of the laser energy are diminished. This phenomenon then allows more efficient use of the laser energy through a more rapid creation of high temperatures and tissue vaporization yet at lower power densities. Such an agent has been sought for the 805 nm diode laser as a means of compensating for the limited power output of the current device.

Greenwell demonstrated a significant increase in the depth of vaporization and the diameter of thermal injury with the 805 nm diode laser and indocyanine green using an in vivo rat liver model [4]. The hepatic uptake of ICG makes it an excellent chromophore for laser irradiation of the

Fig. 1. The endoscopic appearance following control lasing demonstrating minor tissue coagulative surface change.

Fig. 2. Representative example of the endoscopic appearance at the site of lasing after ICG administration revealing a vaporized cavity with surface carbonization.

Fig. 3. Transverse section of the prostate taken from dog #3 treated with the Bard fibre demonstrating the predominantly coagulative lesion at the site treated prior to ICG (arrow) and the more dominant vaporizing effect at the site treated following ICG administration (asterisk).


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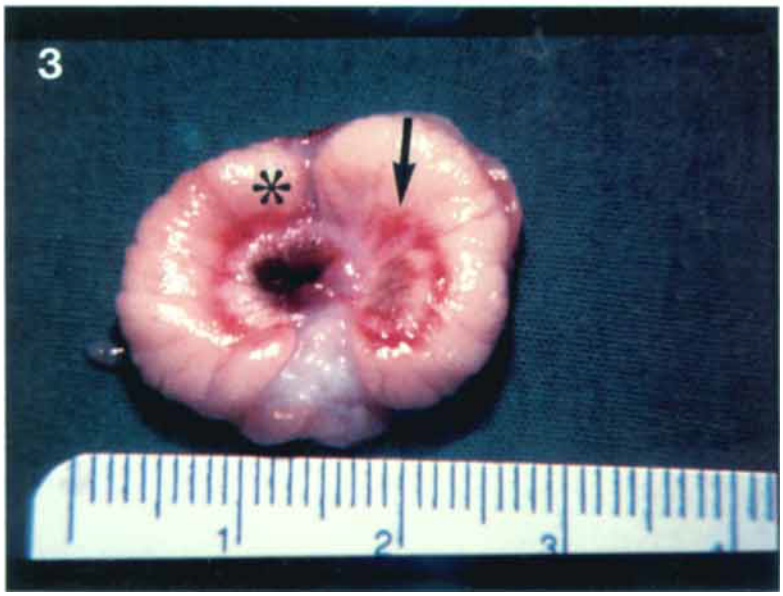
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TABLE 2. Mean Dimensions and Volumes for Coagulative and Vaporized Lesions

Laser fiber	Lasing	Mean lesion dimensions[a] Coagulative zone D	H	L	V	Vaporized cavity D	H	L	V
Sidefocus	pre-ICG	5	4.8	4.2	53.2	0.25	0.25	0.25	0.125
	post-ICG	4.2	3.7	3.7	34.5	1.9	1.9	1.9	3.6
Urolase	pre-ICG	5.8	5.8	6.8	121.5	0.25	0.25	0.25	0.2
	post-ICG	5.8	6.3	6.8	125.2	2.8	2.8	4.5	19.7

[a]D = depth, H = height, L = length (all in mm); V = volume (in mm^3).

TABLE 3. Lesion Volumes-Coagulation Zones

	Range (cc^3)	Mean ± SD (cc^3)
Pre-ICG	47.1–169.5	87.4 ± 51.2
Post-ICG	12.6–230.6	80 ± 69.5*

*$P = 0.81$.

TABLE 4. Lesion Volumes-Vaporized Cavities

	Range (cc^3)	Mean ± SD (cc^3)
Pre-ICG	0–0.78	0.16 ± 0.31
Post-ICG	1–31.4	11.6 ± 11.8*

*$P = 0.015$.

liver. The use of intravenous ICG as a chromophore when irradiating non-hepatic tissues, however, is more problematic. The use of ICG with an 800 nm diode laser has been reported to enhance energy absorption during laser tissue welding [15].

In our study we performed prostate lasings at 4 min and 5.5 min after ICG was given. With an average plasma half-life of 3.4 ± 0.7 min, it was believed that a sufficient portion of the ICG dose was still circulating in plasma [6]. With essentially no uptake into tissue, the amount of ICG within the intravascular compartment of the prostate at the time of lasing was assumed to be equivalent to systemic circulating levels. The observation of more rapid vaporization as well as larger vaporized cavities following ICG administration suggest definite alteration in laser-tissue interaction. These findings were more clearly demonstrated in lasings performed with the Urolase fiber, which produced the largest vaporized cavities. There were no apparent differences in the lesions produced when comparing lasings performed at 4 min or 5.5 min post-ICG.

Despite the different laser-tissue interaction following intravenous ICG, the lesions created remained small in depth and volume. In a previous study, using Nd:YAG free-beam irradiation at 20 W for 60 sec, coagulative lesions ranged 4–8 mm in depth [16]. The coagulative lesions produced by the 805 nm diode laser at 25 W for 60 sec were smaller in this study, suggesting that the 805 nm wavelength is less effective than the Nd:YAG laser at equivalent power output. Even with the addition of the chromophore ICG, although tissue vaporization became the predominant effect, the lesions produced in this canine model remained small. An increase in laser power output, fiber changes allowing increased power density, as well as improving the delivery of ICG to the prostate during laser irradiation are theoretical ways of enhancing tissue effects.

Although the canine model is an accepted in vivo model for the study of laser prostatectomy, the tissue is more heat sensitive and completes the cycle of coagulation, slough, and re-epithelialization more rapidly than the human counterpart. This phenomenon is presumably due to the greater glandular component present in the canine prostate, which may be more susceptible to the effects of heat than the predominantly stromal tissue found in human BPH [17,18]. Since the model is internally consistent, it offers a valid comparison of laser-tissue interaction before and after ICG administration. The overall size of the lesions suggests that the 805 nm diode laser at 25 W is underpowered for free-beam coagulation prostatectomy in humans.

CONCLUSION

We have shown that it is possible to alter the tissue effects with an 805 nm diode laser in the canine prostate with the use of indocyanine green. The 25 W 805 nm diode laser investigated in this study produced small predominantly coagulative lesions prior to the administration of ICG. Following ICG, tissue vaporization was the major effect. Although the laser-tissue interactions were altered by the administration of ICG, the lesions produced remained small. With better uptake of ICG into the prostate and higher laser power output, it may be possible to enhance tissue effects. Although the use of ICG appears limited for large volume prostate tissue destruction, it is an important technique for changing laser-tissue interaction.

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